REMARKS

The Office Action mailed 18 June 2003 has been received and reviewed. Claims 40, 44-46, 50-55, 59-66 and 68 having been amended, the pending claims are claims 1-73. Of these, claims 1-39 and 70-73 stand withdrawn, such that claims 40-69 are presently under examination.

Claims 40, 44-46, 50-55, 59-66 and 68 have been amended to delete the phrase "derived from" a protozoan. Independent claims 40, 46, 52-55 and 61-64 have been amended to recite an immunogenic polypeptide comprising a protozoan polypeptide that is associated with a protozoan cell surface or secreted by a protozoan. Support of this amendment is found, for example, in the specification at page 4, lines 25-27, and page 21, lines 12-15. Claims 62-64 have been amended to recite a multicomponent vaccine. Support for that amendment is found throughout the specification and, for example, at claim 1 as originally filed.

Claim Objections

Claims 40 and 62-64 were objected to because of they are dependent upon a non-elected invention. These claims, along with claims 46, 52-55 and 61, have been rewritten as independent claims. Reconsideration and withdrawal of the objection is respectfully requested.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 40-69 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for therapeutic immunization comprising a vector which encodes TSA-1, does not reasonably provide enablement for a therapeutic immunization with any polypeptide derived from a protozoan. This rejection is respectfully traversed.

The Examiner stated that the specification provides insufficient guidance of how to use which of the multitude of protozoan polypeptides to induce a protective response. Applicants disagree, and reply that there is clear guidance in the specification that polypeptides that are either attached to the protozoan surface or released by the protozoan are known to be

immunogenic. For example, at page 13, line 13, through page 14, line 2, of the specification, it is stated:

> Without intending to be bound by theory, it is believed that proteins anchored by glycosylphosphatidylinositol (GPI) in *T. cruzi* may stimulate all three of these distinct immune responses, thereby generating a broader protection against *T. cruzi* than was previously possible. The failure of previous attempts at vaccination in *T. cruzi* is likely due to the fact that investigators have largely focused on induction of only one or two of these responses, principally antibody production and, to a lesser extent, $CD4^+$ T cell responses. The majority of surface proteins in trypomastigotes and amastigotes of *T. cruzi* are GPI-anchored and many of these surface proteins both elicit and are bound by antibodies. In addition, the GPI anchoring mechanism in *T. cruzi* appears to be very sloppy with a significant portion of proteins targeted for GPI addition being secreted without the addition of a GPI anchor (N. Garg et al., J. Biol. Chem. 272:12482-12491 (1997)). In the case of amastigotes, these secreted proteins lacking GPIs enter the host cell cytoplasm, are presented by class I MHC molecules and elicit the production of CTL responses. On extracellular amastigotes and trypomastigotes, these same proteins in a surface-anchored form sensitize parasites to detection by antibodies specific for the proteins. Lastly, significant class II MHC-restricted, $CD4^+$ T cell reactivity is elicited by GPI-anchored proteins. Thus GPI anchored proteins appear to be excellent targets for stimulation of protective antibody, Th1-biased $CD4^+$ T cell responses, and $CD8^+$ T cell responses.

The specification thus offers guidance as to which polypeptides to select in order to identify polypeptides that would be likely to generate an immune response that is broader than just an antigenic response. Claims 40, 46, 52-55 and 61-64 have been amended to recite an immunogenic polypeptide that comprises a protozoan polypeptide that is associated with a protozoan cell surface or secreted by a protozoan, thereby incorporating this guidance into the claims. Additionally, the specification details methods (e.g., Examples I and II) that the researcher can use to evaluate, without undue experimentation, the immunogenic response in a mouse model generated by the candidate surface-associated or secreted polypeptide. It is respectfully submitted that the skill in the art level is high, and that excessive experimentation would not have been necessary to practice the invention (In re Wands., 858 F.2d 731, 737, 8

USPQ2d 1400, 1404 (Fed. Cir. 1988)). Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is, accordingly, requested.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 40-69 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that claims 40-69 are vague and indefinite in the use of the phrase "derived." This rejection is respectfully traversed.

Claims 40, 44-46, 50-55, 59-66 and 68 have been amended to delete the phrase "derived from" a protozoan. Independent claims 40, 46, 52-55 and 61-64 now recite an immunogenic polypeptide comprising a protozoan polypeptide that is associated with a protozoan cell surface or secreted by a protozoan. It is submitted that this amendment obviates the rejection. Reconsideration and withdrawal of the rejection of claims 40-69 under 35 U.S.C. §112, second paragraph, is respectfully requested.

Rejection under 35 U.S.C. §102

The Examiner rejected claims 61-64 under 35 U.S.C. §102(a) as being anticipated by Wizel et al. (Infection and Immunity, Vol. 66, No. 11, November 1998, pp. 5073-5081). The Examiner rejected claims 61-64 under 35 U.S.C. §102(a) as being anticipated by Costa et al. (Vaccine, Vol. 16, No. 8, 1998, pp. 768-774). The Examiner rejected claims 61-64 under 35 U.S.C. §102(b) as being anticipated by Reed (U.S. Patent No. 5,304,371). This rejection is respectfully traversed.

Claim 61 recites a multicomponent vaccine that is effective prevent the death of the mammal after subsequent infection by the protozoan. Claims 62-64 have also been amended to recite a multicomponent vaccine. Costa et al., and Reed et al. both teach only a single component vaccine, therefore they do not anticipate the invention of claims 61-64. Wizel et al. report the use of adoptive transfer of T cells to provide immunological protection in mice against subsequent challenge with *T. cruzi* infection, but do not report the actual preparation or use of a

multicomponent polypeptide or polynucleotide vaccine. Although Wizel et al. do state (Wizel et al., at page 6128) that "[v]accines against Chagas' disease will most likely include, among other components, multiple determinants from *T. cruzi* trypomastigote and amastigote Ags that induce protective CD8+ CTL capable of recognizing and preventing the parasitized cell from sustaining a productive infection" and that the "key to prevention or amelioration of Chagas' disease is to achieve a reduction in parasite load through chemotherapeutics of anti-parasite immunotherapies," only two *T. cruzi* antigens that are targets of CD8+ T cells are taught, and the mice were not vaccinated. It is respectfully submitted that Wizel et al. is therefore not an enabling disclosure.

Reconsideration and withdrawal of claims 61-64 under 35 U.S.C. §102(a) is respectfully requested.

Summary

It is respectfully submitted that the pending claims 40-69 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.10:

"Express Mail" mailing label number: EV 073 687 599 US Date of Deposit: December 18, 2003

I hereby certify that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: _____ Name: Rachel Baglindi-Graham